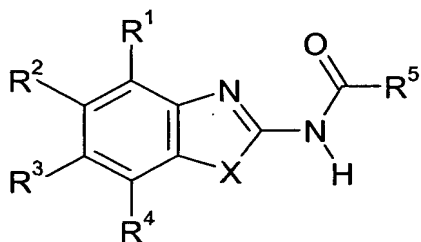


We claim:

1. A compound of formula I,



5

wherein:

R<sup>1</sup> and R<sup>4</sup> are each, independently,

10

H;

C<sub>1</sub>-C<sub>10</sub>-alkyl, C<sub>2</sub>-C<sub>10</sub>-alkenyl or C<sub>2</sub>-C<sub>10</sub>-alkynyl, each of which is optionally substituted one or more times by F, OH, C<sub>1</sub>-C<sub>8</sub>-alkoxy, C<sub>1</sub>-C<sub>8</sub>-alkylmercapto, -CN, COOR<sup>6</sup>, CONR<sup>7</sup>R<sup>8</sup>, phenyl or heteroaryl, wherein the phenyl and heteroaryl are each independently optionally substituted one or more times by halogen, -CN, C<sub>1</sub>-C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy or CF<sub>3</sub>;

15

phenyl or heteroaryl, each of which is optionally substituted one or more times by halogen, -CN, C<sub>1</sub>-C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy or CF<sub>3</sub>;

COR<sup>9</sup>;

CONR<sup>10</sup>R<sup>11</sup>;

20

COOR<sup>12</sup>;

CF<sub>3</sub>;

halogen;

-CN;

NR<sup>13</sup>R<sup>14</sup>;

25

OR<sup>15</sup>;

S(O)<sub>m</sub>R<sup>16</sup>;

SO<sub>2</sub>NR<sup>17</sup>R<sup>18</sup>; or

NO<sub>2</sub>;

R<sup>2</sup> and R<sup>3</sup> are each, independently,

H;

5 halogen;

-CN;

C<sub>1</sub>-C<sub>10</sub>-alkyl, optionally substituted one or more times by OH, phenyl, or heteroaryl;

OH;

10 C<sub>1</sub>-C<sub>10</sub>-alkoxy;

phenoxy;

S(O)<sub>m</sub>R<sup>19</sup>;

CF<sub>3</sub>;

NO<sub>2</sub>;

15 C<sub>1</sub>-C<sub>10</sub>-alkylamino;

di(C<sub>1</sub>-C<sub>10</sub>-alkyl)amino;

(C<sub>1</sub>-C<sub>6</sub>-alkyl)-CONH-;

phenyl-CONH- or phenyl-SO<sub>2</sub>-O-, wherein the phenyl is optionally substituted one or more times by halogen, -CN, methyl or methoxy;

20 C<sub>1</sub>-C<sub>6</sub>-alkyl-SO<sub>2</sub>-O-;

(C<sub>1</sub>-C<sub>6</sub>-alkyl)-CO-, wherein the C<sub>1</sub>-C<sub>6</sub>-alkyl is optionally substituted one or more times by F, di(C<sub>1</sub>-C<sub>3</sub>-alkyl)amino, pyrrolidinyl or piperidinyl; or

phenyl-CO-, wherein the phenyl is optionally substituted one or more times by C<sub>1</sub>-C<sub>3</sub>-alkyl, halogen or methoxy;

25

R<sup>5</sup> is Ar or Heter, each of which is optionally substituted one or more times by

halogen;

-CN;

NH<sub>2</sub>;

30 C<sub>1</sub>-C<sub>10</sub>-alkyl, C<sub>2</sub>-C<sub>10</sub>-alkenyl, C<sub>2</sub>-C<sub>10</sub>-alkynyl, C<sub>1</sub>-C<sub>10</sub>-alkoxy, C<sub>1</sub>-C<sub>10</sub>-alkylamino or di(C<sub>1</sub>-C<sub>10</sub>-alkyl)amino, wherein the alkyl, alkenyl, alkynyl

and alkoxy are each independently optionally substituted one or more times by F, OH, C<sub>1</sub>-C<sub>8</sub>-alkoxy, aryloxy, C<sub>1</sub>-C<sub>8</sub>-alkylmercapto, NH<sub>2</sub>, C<sub>1</sub>-C<sub>8</sub>-alkylamino or di(C<sub>1</sub>-C<sub>8</sub>-alkyl)amino;

C<sub>3</sub>-C<sub>5</sub>-alkandiyl;

5

phenyl;

heteroaryl;

aryl-substituted or heteroaryl-substituted C<sub>1</sub>-C<sub>4</sub>-alkyl;

CF<sub>3</sub>;

NO<sub>2</sub>;

10

OH;

phenoxy;

benzyloxy;

(C<sub>1</sub>-C<sub>10</sub>-alkyl)-COO-;

S(O)<sub>m</sub>R<sup>20</sup>;

15

SH;

phenylamino;

benzylamino;

(C<sub>1</sub>-C<sub>10</sub>-alkyl)-CONH-;

(C<sub>1</sub>-C<sub>10</sub>-alkyl)-CO-N(C<sub>1</sub>-C<sub>4</sub>-alkyl)-;

20

phenyl-CONH-;

phenyl-CO-N(C<sub>1</sub>-C<sub>4</sub>-alkyl)-;

heteroaryl-CONH-;

heteroaryl-CO-N(C<sub>1</sub>-C<sub>4</sub>-alkyl)-;

(C<sub>1</sub>-C<sub>10</sub>-alkyl)-CO-;

25

phenyl-CO-;

heteroaryl-CO-;

CF<sub>3</sub>-CO-;

-OCH<sub>2</sub>O-;

-OCF<sub>2</sub>O-;

30

-OCH<sub>2</sub>CH<sub>2</sub>O-;

-CH<sub>2</sub>CH<sub>2</sub>O-;

COOR<sup>21</sup>;

CONR<sup>22</sup>R<sup>23</sup>;

C(NH)-NH<sub>2</sub>;

SO<sub>2</sub>NR<sup>24</sup>R<sup>25</sup>;

5 R<sup>26</sup>SO<sub>2</sub>NH-;

R<sup>27</sup>SO<sub>2</sub>N(C<sub>1</sub>-C<sub>6</sub>-alkyl)-; or

a residue of a saturated or unsaturated aliphatic, monocyclic 5-

membered to 7-membered heterocycle containing 1, 2 or 3

heteroatoms selected from the group consisting of N, O and S, wherein

10 the heterocycle is optionally substituted one or more times by halogen,

C<sub>1</sub>-C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy, OH, oxo or CF<sub>3</sub>, and the heterocycle is

optionally condensed to the group Ar or the group Hetar;

wherein all aryl, heteroaryl, phenyl, aryl-containing, heteroaryl-containing and phenyl-containing groups, which are optionally present in the said substituents

15 of the said group Ar or the said group Hetar, can be substituted by one or more substituents selected from the group consisting of halogens, -CN, C<sub>1</sub>-C<sub>3</sub>-alkyl, OH, C<sub>1</sub>-C<sub>3</sub>-alkoxy, and CF<sub>3</sub>;

R<sup>6</sup> is H;

20 C<sub>1</sub>-C<sub>10</sub>-alkyl, optionally substituted one or more times by F, C<sub>1</sub>-C<sub>8</sub>-alkoxy or di(C<sub>1</sub>-C<sub>8</sub>-alkyl)amino;

aryl-(C<sub>1</sub>-C<sub>4</sub>-alkyl)- or heteroaryl-(C<sub>1</sub>-C<sub>4</sub>-alkyl)- either of which is optionally substituted one or more times by halogen, C<sub>1</sub>-C<sub>4</sub>-alkyl, C<sub>1</sub>-C<sub>4</sub>-alkoxy or di(C<sub>1</sub>-C<sub>6</sub>-alkyl)amino;

25

R<sup>7</sup> is H;

C<sub>1</sub>-C<sub>10</sub>-alkyl, optionally substituted one or more times by F, C<sub>1</sub>-C<sub>8</sub>-alkoxy, di(C<sub>1</sub>-C<sub>8</sub>-alkyl)amino or phenyl; or

30 phenyl, indanyl or heteroaryl, each of which is optionally substituted one or more times by halogen, -CN, C<sub>1</sub>-C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy or CF<sub>3</sub>;

R<sup>8</sup> is H or C<sub>1</sub>-C<sub>10</sub>-alkyl;

R<sup>9</sup> is C<sub>1</sub>-C<sub>10</sub>-alkyl, optionally substituted one or more times by F, C<sub>1</sub>-C<sub>4</sub>-alkoxy or di(C<sub>1</sub>-C<sub>3</sub>-alkyl)amino; or

5 phenyl or heteroaryl, each of which is optionally substituted one or more times by C<sub>1</sub>-C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy, halogen, -CN or CF<sub>3</sub>;

R<sup>10</sup>, independently from R<sup>7</sup>, is R<sup>7</sup>;

10 R<sup>11</sup>, independently from R<sup>8</sup>, is R<sup>8</sup>;

R<sup>12</sup>, independently from R<sup>6</sup>, is R<sup>6</sup>;

R<sup>13</sup> is H;

15 C<sub>1</sub>-C<sub>6</sub>-alkyl; or  
phenyl, benzyl, heteroaryl, (C<sub>1</sub>-C<sub>6</sub>-alkyl)-CO-, phenyl-CO-, or heteroaryl-CO-,  
each of which is optionally substituted one or more times by halogen, -CN, C<sub>1</sub>-  
C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy or CF<sub>3</sub>;

20 R<sup>14</sup>, independently from R<sup>13</sup>, is R<sup>13</sup>;

R<sup>15</sup> is H;

C<sub>1</sub>-C<sub>10</sub>-alkyl;

(C<sub>1</sub>-C<sub>3</sub>-alkoxy)-C<sub>1</sub>-C<sub>3</sub>-alkyl-;

25 benzyl, phenyl or heteroaryl, each of which is optionally substituted one or  
more times by halogen, -CN, C<sub>1</sub>-C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy or CF<sub>3</sub>;

R<sup>16</sup> is C<sub>1</sub>-C<sub>10</sub>-alkyl, optionally substituted one or more times by F, OH, C<sub>1</sub>-C<sub>8</sub>-alkoxy,  
aryloxy, C<sub>1</sub>-C<sub>8</sub>-alkylmercapto, C<sub>1</sub>-C<sub>8</sub>-alkylamino or di(C<sub>1</sub>-C<sub>8</sub>-alkyl)amino;

30 CF<sub>3</sub>; or

phenyl or heteroaryl, each of which is optionally substituted one or more times by halogen, -CN, C<sub>1</sub>-C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy or CF<sub>3</sub>;

R<sup>17</sup>, independently from R<sup>7</sup>, is R<sup>7</sup>;

5

R<sup>18</sup>, independently from R<sup>8</sup>, is R<sup>8</sup>;

R<sup>19</sup>, independently from R<sup>16</sup>, is R<sup>16</sup>;

10 R<sup>20</sup>, independently from R<sup>16</sup>, is R<sup>16</sup>;

R<sup>21</sup>, independently from R<sup>6</sup>, is R<sup>6</sup>;

R<sup>22</sup>, independently from R<sup>7</sup>, is R<sup>7</sup>;

15

R<sup>23</sup>, independently from R<sup>8</sup>, is R<sup>8</sup>;

R<sup>24</sup>, independently from R<sup>7</sup>, is R<sup>7</sup>;

20 R<sup>25</sup>, independently from R<sup>8</sup>, is R<sup>8</sup>;

R<sup>26</sup>, independently from R<sup>16</sup>, is R<sup>16</sup>;

R<sup>27</sup>, independently from R<sup>16</sup>, is R<sup>16</sup>;

25

R<sup>30</sup> is H;

C<sub>1</sub>-C<sub>10</sub>-alkyl, C<sub>2</sub>-C<sub>10</sub>-alkenyl or C<sub>2</sub>-C<sub>10</sub>-alkynyl, each of which is optionally substituted one or more times by F, OH, C<sub>1</sub>-C<sub>8</sub>-alkoxy, C<sub>1</sub>-C<sub>8</sub>-alkylmercapto, -CN, COOR<sup>31</sup>, CONR<sup>32</sup>R<sup>33</sup>, NR<sup>34</sup>R<sup>35</sup>, (C<sub>1</sub>-C<sub>8</sub>-alkyl)-CONH-, (C<sub>1</sub>-C<sub>8</sub>-alkoxy)-CONH-, benzyloxy-CONH-, phenyl or heteroaryl, wherein the phenyl and

30

heteroaryl are each independently optionally substituted one or more times by halogen, -CN, C<sub>1</sub>-C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy or CF<sub>3</sub>; or phenyl or heteroaryl, each of which is optionally substituted one or more times by halogen, -CN, C<sub>1</sub>-C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy or CF<sub>3</sub>;

5

R<sup>31</sup>, independently from R<sup>6</sup>, is R<sup>6</sup>;

R<sup>32</sup>, independently from R<sup>6</sup>, is R<sup>6</sup>;

10 

R<sup>33</sup>, independently from R<sup>6</sup>, is R<sup>6</sup>;

R<sup>34</sup>, independently from R<sup>6</sup>, is R<sup>6</sup>;

R<sup>35</sup>, independently from R<sup>6</sup>, is R<sup>6</sup>;

15

X is NR<sup>30</sup>, S, O, CH=CH, N=CH or CH=N;

heteroaryl is a residue of a 5-membered to 10-membered, aromatic, monocyclic or bicyclic heterocycle containing one or more heteroatoms selected from the group consisting of N, O and S;

20

the group Hetar is a residue of a 5-membered to 10-membered, aromatic, monocyclic or bicyclic heterocycle containing one or more heteroatoms selected from the group consisting of N, O and S;

25

aryl is phenyl, naphth-1-yl or naphth-2-yl;

the group Ar is phenyl, naphth-1-yl or naphth-2-yl; and

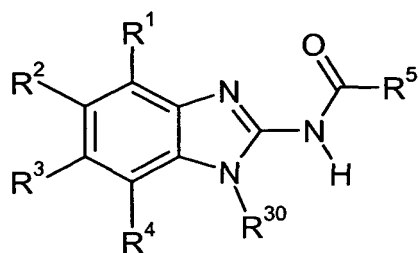
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m is 0, 1 or 2;

or a stereoisomer or a mixture of stereoisomers thereof in any ratio, or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 of formula Ia

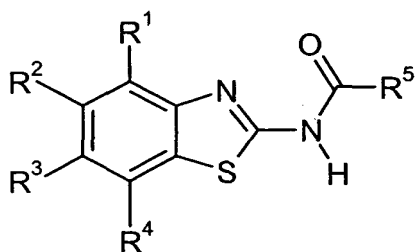
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Ia

wherein R<sup>30</sup> is methyl.

10 3. A compound according to claim 1 of formula Ic



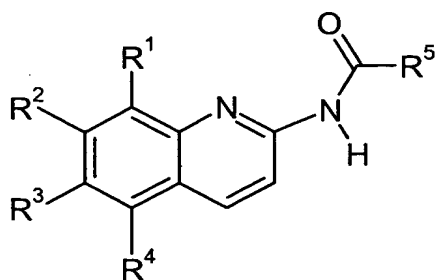
Ic

4. A compound according to claim 1 of formula Id

15

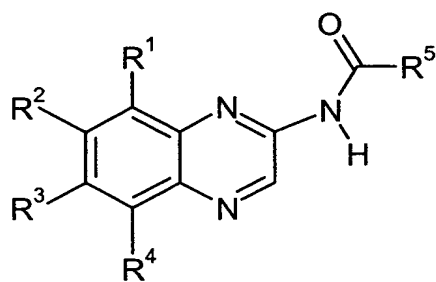


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Id

5. A compound according to claim 1 of formula Ie



Ie

5

6. A compound according to claim 1, wherein:

R<sup>1</sup> and R<sup>4</sup> are each, independently,

H;

10 Halogen; or

C<sub>1</sub>-C<sub>4</sub>-alkyl;

and

R<sup>2</sup> and R<sup>3</sup> are each, independently,

H;

15 Halogen; or

C<sub>1</sub>-C<sub>4</sub>-alkyl.

7. A compound according to claim 1, wherein:

R<sup>5</sup> is phenyl or Heter, each of which is optionally substituted one or more times by

20 halogen;

- CN;  
 NH<sub>2</sub>;  
 C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, C<sub>2</sub>-C<sub>6</sub>-alkynyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy, C<sub>1</sub>-C<sub>4</sub>-alkylamino or di(C<sub>1</sub>-C<sub>4</sub>-alkyl)amino, each of which is optionally substituted one or more times by F, C<sub>1</sub>-C<sub>3</sub>-alkoxy, C<sub>1</sub>-C<sub>3</sub>-alkylmercapto or NH<sub>2</sub>;  
 C<sub>3</sub>-C<sub>5</sub>-alkandiyl;  
 phenyl;  
 heteroaryl;  
 phenyl-substituted or heteroaryl-substituted C<sub>1</sub>-C<sub>2</sub>-alkyl;  
 CF<sub>3</sub>;  
 OH;  
 (C<sub>1</sub>-C<sub>4</sub>-alkyl)-COO;  
 S(O)<sub>m</sub>-(C<sub>1</sub>-C<sub>4</sub>)-alkyl;  
 (C<sub>1</sub>-C<sub>4</sub>-alkyl)-CONH-;  
 (C<sub>1</sub>-C<sub>4</sub>-alkyl)-CON(C<sub>1</sub>-C<sub>4</sub>-alkyl)-;  
 (C<sub>1</sub>-C<sub>4</sub>-alkyl)-CO-;  
 phenyl-CO-;  
 heteroaryl-CO-;  
 CF<sub>3</sub>-CO-;  
 -OCH<sub>2</sub>O-;  
 -OCF<sub>2</sub>O-;  
 -OCH<sub>2</sub>CH<sub>2</sub>O-;  
 -CH<sub>2</sub>CH<sub>2</sub>O-;  
 COO(C<sub>1</sub>-C<sub>6</sub>-alkyl);  
 -CONH<sub>2</sub>;  
 -CONH(C<sub>1</sub>-C<sub>4</sub>-alkyl);  
 -CON(di(C<sub>1</sub>-C<sub>4</sub>-alkyl));  
 -C(NH)NH<sub>2</sub>;  
 -SO<sub>2</sub>NH<sub>2</sub>;  
 -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub>-alkyl);

-SO<sub>2</sub>NH(phenyl);  
 -SO<sub>2</sub>N(di(C<sub>1</sub>-C<sub>4</sub>-alkyl));  
 (C<sub>1</sub>-C<sub>4</sub>-alkyl)-SO<sub>2</sub>NH-;  
 (C<sub>1</sub>-C<sub>4</sub>-alkyl)-SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub>-alkyl)-; or

- 5 a residue of a saturated or unsaturated aliphatic, mononuclear 5-membered to 7-membered heterocycle containing 1, 2 or 3 heteroatoms selected from the group consisting of N, O and S, wherein the heterocycle is optionally substituted one or more times by halogen, C<sub>1</sub>-C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy, OH, oxo or CF<sub>3</sub>, and the heterocycle is optionally
- 10 condensed to the said phenyl or the said group Hetar;
- wherein all heteroaryl, phenyl, heteroaryl-containing and phenyl-containing groups, which are optionally present in the said substituents of the said phenyl or the said group Hetar, can be substituted by one or more substituents selected from the group consisting of halogen, -CN, C<sub>1</sub>-C<sub>3</sub>-alkyl, OH, C<sub>1</sub>-C<sub>3</sub>-
- 15 alkoxy, and CF<sub>3</sub>.

8. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound according to claim 1 and a pharmaceutically acceptable carrier.

- 20 9. A method for the stimulation of the expression of endothelial NO synthase, in a patient in need thereof, comprising administering to the patient a pharmaceutically effective amount of a compound according to claim 1.

10. A method for the treatment of cardiovascular diseases, stable or unstable angina
- 25 pectoris, coronary heart disease, Prinzmetal angina, acute coronary syndrome, heart failure, myocardial infarction, stroke, thrombosis, peripheral artery occlusive disease, endothelial dysfunction, atherosclerosis, restenosis, endothel damage after PTCA, hypertension, essential hypertension, pulmonary hypertension, secondary hypertension, renovascular hypertension, chronic glomerulonephritis, erectile
- 30 dysfunction, ventricular arrhythmia, diabetes, diabetes complications, nephropathy, retinopathy, angiogenesis, asthma bronchiale, chronic renal failure, cirrhosis of the

liver, osteoporosis, restricted memory performance or a restricted ability to learn, or for the lowering of cardiovascular risk of postmenopausal women or of women taking contraceptives, in a patient in need thereof, comprising administering to the patient a pharmaceutically effective amount of a compound according to claim 1.